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The National Professional Society of Pharmacists

June 21, 1999

Dockets Management Branch (HFA-305)
Food and Drug Administration
Room 1061
5630 Fisher Lane
Rockville, MD 20852

Re: Draft Guidance on Placing the FDA Therapeutic Equivalence Code on Prescription Drug Labels and Labeling
[Docket No. 98D-1266]

Dear Sir or Madam:

The American Pharmaceutical Association (APhA), the national professional society of pharmacists, appreciates the opportunity to comment on the "Draft Guidance for Industry on Placing the Therapeutic Equivalence Code on Prescription Drug Labels and Labeling." APhA's 53,000 members include pharmacy practitioners, pharmaceutical scientists, pharmacy students, pharmacy technicians, and others interested in advancing the profession.

APhA shares FDA's concern that health care professionals need better information addressing whether a specific drug is therapeutically equivalent to another pharmaceutically equivalent drug product. In recognition of the need for better information, APhA published a "Special Report, Evaluating Therapeutic Equivalence: A Pharmacist's Guide" to help pharmacists meet their responsibility for drug product selection in the face of competing pressures to make choices that are both cost-effective and best for patients.

The *intent* of this Draft Guidance on placing therapeutic equivalent codes on prescription drug labels and labeling seeks to contribute to the accurate and safe selection of drug products by health care practitioners. APhA strongly supports systems and mechanisms that aid in the prevention of medication errors. Pharmacists are typically the last line of defense among health care professionals to ensure that patients receive proper medications. The Draft Guidance document would allow the placement of the therapeutic codes provided in the *Approved Prescription Drug Products with Therapeutic Equivalency Evaluations List* (also known as the *Orange Book*) on drug product labeling and product container labels. APhA is concerned, however, that implementing this guidance document will potentially undermine FDA's intent of reducing medication errors and *contribute* to medication errors.

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Many health care practitioners are likely to be unfamiliar with therapeutic equivalency codes. The labeling option allowed by the draft guideline is likely insufficient to correct this lack of familiarity. Under the Draft Guidance, for example, a manufacturer of a brand product may indicate that the product is not therapeutically equivalent to another distinct product. When the labeling for Konakion ® states "this product is BP to Aquamephyton®" without defining the two-letter code on the labeling, the health care practitioner likely would still need to refer to the *Orange Book* for clarification. The usefulness of placing therapeutic equivalency codes on a product label therefore may serve only a limited pool of health care practitioners – those already familiar with the nomenclature.

While the confusion for health professionals represents one concern, patients may potentially be misled as well. In the event a prescription is presented to a patient in packaging which includes original labeling, any series of equivalence codes may imply equivalency when in fact, the alternate is the case.

In addition to the potential confusion of this new information, this information would appear on what some would characterize a cluttered label. The Draft Guidance document pertains to all prescription drug product labels and labeling, including injectable products. Injectables are frequently packaged in small containers with limited space on the labels. A joint United States Pharmacopoeia (USP) and FDA subcommittee published recommendations for label simplification in 1994 to assure that nothing detracts from the primary purpose of a drug label.

One important recommendation from the joint subcommittee was implemented in the FDA Modernization Act (FDAMA) of 1997. Legend statements such as "Warning may be habit forming" and "Federal law prohibits dispensing without prescription," for example, were replaced with an "R_x only" symbol, from some labeling to reduce unnecessary clutter. Including therapeutic equivalency codes on labeling may counter the work of the joint subcommittee to reduce clutter on labeling and to decrease product confusion.

While the federal legend statement revision was intended to decrease the number of words on labeling on prescription products, the Therapeutic Equivalence Draft Guidance *increases* the number of words on the container label. Implementing such a therapeutic equivalency rating would require adding two full sentences to the container label, or at a minimum, one phrase and one sentence. The addition of the therapeutic equivalency code would require more product container labeling space while providing potentially confusing information.

The Draft Guidance further asserts that "The use of therapeutic equivalency evaluations in drug product labeling will . . . help state health agencies in the administration of their drug product selection laws." APhA is concerned that the guidance document suggests

that these state health agencies should review the basic information provided on product bottles and package inserts to determine a state's drug product selection law(s). Such important decisions should be made only with full product information including the important information in the *Orange Book.* The Draft Guidance document recognizes, "Drug information, as presented by the *Orange Book*, is dynamic and complex and is subject to changing conditions." On such *complex* and important issues as administering state drug product selection laws, APhA would hope that state agencies use the complete information provided in the *Orange Book* versus the basic therapeutic equivalency codes and minimal information on labels.

Further problems are created by the potential for the therapeutic equivalency information to change. Once a therapeutic equivalency claim on the labeling of a product container becomes inaccurate – "subject to the complex and . . .changing conditions" of the *Orange Book* – and the product has been distributed to health professionals, action will be needed to correct the product's mislabeled equivalency claim. The manufacturer may have to recall a drug that is in the distribution system since the label information on the product container is incorrect. Or, if a manufacturer is not required to recall a drug in distribution, the potential for medication error may increase if a product label asserts a mislabeled therapeutic equivalence rating.

APhA agrees that health professionals and the public need better information to promote safe and effective use of therapeutically equivalent products. However, the space on product labeling is limited and implementing this Draft Guidance has the potential of confusing health care professionals and the public about the meaning of the coding system. APhA recommends that therapeutic equivalency codes can better serve the purpose of reducing medical errors by placing them on package inserts with a description of the equivalency coding system and a notation for health professionals to refer to the *Orange Book* for further information.

The *Orange Book* provides current, comprehensive and convenient therapeutic equivalency code information in both the hard copy version and via access on the FDA web site. Brief and potentially confusing coding system statements printed on the product container cannot substitute the information offered in the *Orange Book.*

APhA also has strong concern that there is no provision for field testing by health care professionals or examination by human factor experts to determine the effectiveness of the labeling system before its large scale adoption. Should problems arise with the coding system, they can be addressed quickly in a defined testing environment. Such testing should be an integral component of implementing any large-scale labeling modification.

In conclusion, APhA agrees with the *intent* of the Draft Guidance document, however, its potential safety implementations raise too many concerns for the Association to advocate for its adoption. Therapeutic equivalency codes on prescription drug labels and labeling without a description of the equivalency coding system and a notation for health professionals to refer to the *Orange Book* for further information will likely confuse health care providers and patients. If anywhere, therapeutic equivalency codes should appear on package inserts with a description of the equivalency coding system and a notation for health professionals to refer to the *Orange Book* for further information to help prevent medication errors.

APhA also requests that the Association be officially affiliated with the comments submitted by the National Coordinating Council for Medication Error Reporting and Prevention.

The members of APhA appreciate your consideration of these comments. Please contact Jay Baumgartner (202/429-7538) or Susan Winckler (202/429-7533) of my staff if you need additional information or have any questions.

Sincerely,

John A. Gans, PharmD
Executive Vice President and Chief Executive Officer

Enclosure

JAG/jkb

cc: Lucinda L. Maine, Ph.D., Senior Vice President of Professional and Public Affairs
Susan C. Winckler, Pharmacist, Director of Policy and Legislation
Mr. Jay K. Baumgartner, Director of Regulatory Affairs

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